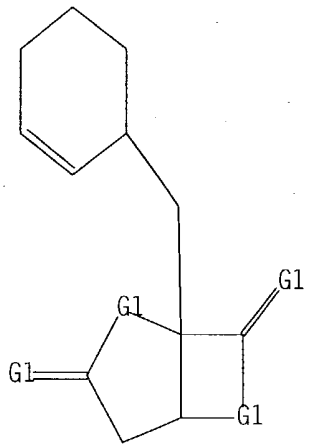
=> d his

(FILE 'HOME' ENTERED AT 11:30:18 ON 21 DEC 2004)

FILE 'REGISTRY' ENTERED AT 11:30:23 ON 21 DEC 2004
L1 STRUCTURE UPLOADED
L2 0 S L1
L3 7 S L1 FULL

FILE 'CAPLUS' ENTERED AT 11:30:52 ON 21 DEC 2004
L4 7 S L3

=> d que l4 stat
L1 STR



G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.
L3 7 SEA FILE=REGISTRY SSS FUL L1
L4 7 SEA FILE=CAPLUS ABB=ON PLU=ON L3

=> d 1-7 ibib iabs hitstr

L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:701941 CAPLUS
DOCUMENT NUMBER: 141:224070
TITLE: Preparation of 6-oxa-2-azabicyclo[3.2.0]heptane-3,7-dione (salinosporamide) derivatives for inhibition of proteasomes and treatment of proteasome-mediated diseases
INVENTOR(S): Stadler, Marc; Seip, Stephan; Mueller, Hartwig; Mayer-Bartschmid, Anke; Bruening, Michael-Alexander; Benet-Buchholz, Jordi; Togame, Hiroko; Dodo, Reiko; Reinemer, Peter; Bacon, Kevin; Fuchikami, Kinji; Matsukawa, Satoko; Urbahns, Klaus
PATENT ASSIGNEE(S): Bayer Healthcare AG, Germany; et al.
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004071382	A2	20040826	WO 2004-EP1097	20040206

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-3495 A 20030214
EP 2003-7594 A 20030402
OTHER SOURCE(S): MARPAT 141:224070
GRAPHIC IMAGE:

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

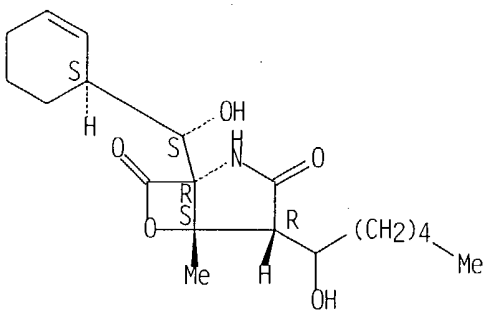
ABSTRACT:
The title compound I and II [R1 = H, OH, methylcarbonyloxy; R2, R5 = cyclohexyl or cyclohexy-2-enyl, wherein cyclohexyl can be substituted with 0-2 hydroxy groups; R3, R6 = H or OH; R4 = H or OH; R7 = OH, cysteinyl, acetylaminoethylsulfanyl, methoxycarbonylethylsulfanyl, etc.] were prepared via fermentation of an Actinomycete of the genus Streptomyces and subsequently derivatized. Compds. I and II are useful as inhibitors of proteasomes for the treatment of proteasome-mediated diseases, such as asthma or cancer. For

example, compound III was isolated from the fermentation exts. and its structure was established by HPLC-MS and multi-dimensional NMR techniques. The latter showed an IC50 =1 nM in the proteasome inhibition assay.

IT **744200-67-7P 744200-68-8P**
RL: PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Preparation of 6-oxa-2-azabicyclo[3.2.0]heptane-3,7-dione (salinosporamide) derivs. for inhibition of proteasomes and treatment of proteasome-mediated diseases)

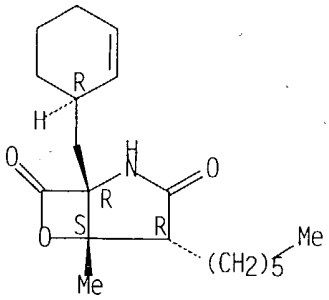
RN 744200-67-7 CAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-(1-hydroxyhexyl)-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 744200-68-8 CAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(1R)-2-cyclohexen-1-ylmethyl]-4-hexyl-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



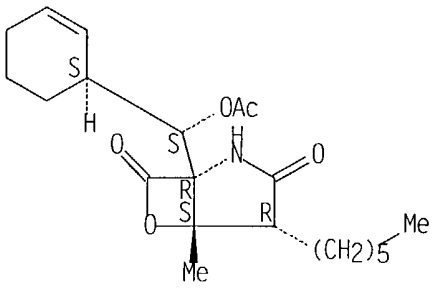
IT **744200-75-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Preparation of 6-oxa-2-azabicyclo[3.2.0]heptane-3,7-dione (salinosporamide) derivs. for inhibition of proteasomes and treatment of

proteasome-mediated diseases)

RN 744200-75-7 CAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(acetyloxy)(1S)-2-cyclohexen-1-ylmethyl]-4-hexyl-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **744200-66-6P**

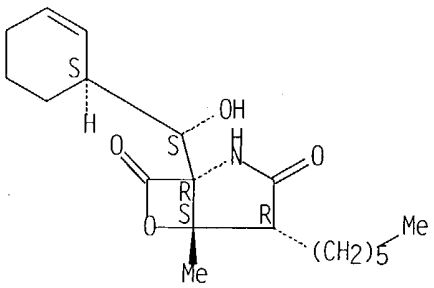
RL: PAC (Pharmacological activity); PRP (Properties); PUR (Purification or recovery); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(crystal structure; Preparation of 6-oxa-2-azabicyclo[3.2.0]heptane-3,7-dione (salinosporamide) derivs. for inhibition of proteasomes and treatment of proteasome-mediated diseases)

RN 744200-66-6 CAPLUS

CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-(1S)-2-cyclohexen-1-ylhydroxymethyl]-4-hexyl-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



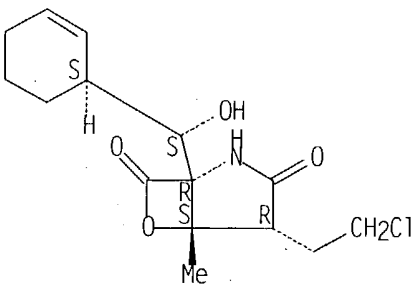
L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:570502 CAPLUS
DOCUMENT NUMBER: 141:105361
TITLE: Salinosporamides and methods for use thereof
INVENTOR(S): Fenical, William; Jensen, Paul; Mincer, Tracy; Feling, Robert H. R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 26 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004138196	A1	20040715	US 2003-600854		20030620
PRIORITY APPLN. INFO.:			US 2002-391314P	P	20020624

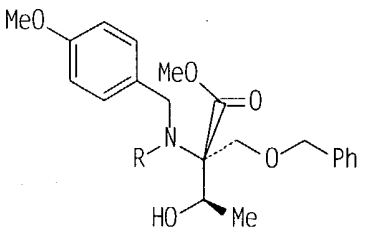
OTHER SOURCE(S): MARPAT 141:105361
ABSTRACT:
The present invention is based on the discovery that certain fermentation products of the marine actinomycete strains CNB392 and CNB476 are effective inhibitors of hyperproliferative mammalian cells. The CNB392 and CNB476 strains lie within the family Micromonosporaceae, and the generic epithet Salinospora has been proposed for this obligate marine group. The reaction products produced by this strain are classified as salinosporamides, and are particularly advantageous in treating neoplastic disorders due to their low mol. weight, low IC 50 values, high pharmaceutical potency, and selectivity for cancer cells over fungi.

IT **437742-34-2P**, Salinosporamide A
RL: BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(salinosporamides and anticancer use thereof)
RN 437742-34-2 CAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-[(1S)-2-cyclohexen-1-yl]hydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:340603 CAPLUS
DOCUMENT NUMBER: 141:54117
TITLE: A Simple Stereocontrolled Synthesis of Salinosporamide A
AUTHOR(S): Reddy, Leleti Rajender; Saravanan, P.; Corey, E. J.
CORPORATE SOURCE: Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA, 02138, USA
SOURCE: Journal of the American Chemical Society (2004), 126(20), 6230-6231
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:54117
GRAPHIC IMAGE:



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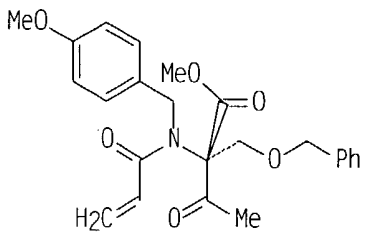

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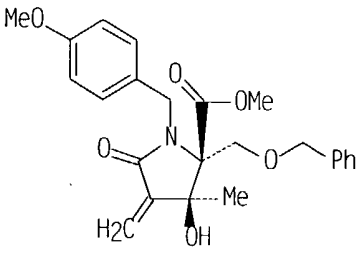
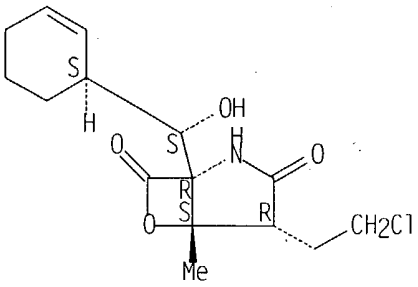


III

ABSTRACT:
A simple and effective stereocontrolled synthesis of salinosporamide A has been developed. Of special note is the direct conversion of amino(benzyloxymethyl)hydroxybutanoate I (R = H) to acryloyl derivative I (R = COCH:CH2). Also, quinuclidine proved to be superior to other bases in the cyclization of oxybutanoate II to oxopyrrolidinecarboxylate III. This process, the first synthesis of salinosporamide A, is capable of providing the compound in substantial quantities for further biol. studies. Salinosporamide A was of special interest as a synthetic target because of its potent in vitro cytotoxic activity against many tumor cell lines (IC50 values of 10 nM or less).

IT **437742-34-2P**, Salinosporamide A
RL: SPN (Synthetic preparation); PREP (Preparation)
(asym. synthesis of salinosporamide A)
RN 437742-34-2 CAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-[(1S)-2-cyclohexen-1-yl]hydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

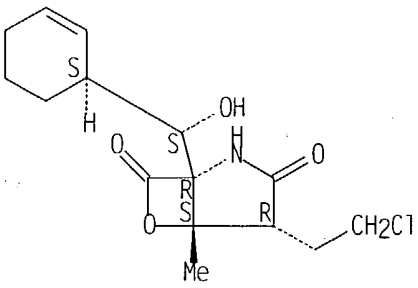


REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:101938 CAPLUS
DOCUMENT NUMBER: 139:81745
TITLE: Salinosporamide A: a highly cytotoxic proteasome inhibitor from a novel microbial source, a marine bacterium of the new genus Salinospora
AUTHOR(S): Feling, Robert H.; Buchanan, Greg O.; Mincer, Tracy J.; Kauffman, Christopher A.; Jensen, Paul R.; Fenical, William
CORPORATE SOURCE: Center for Marine Biotechnology and Biomedicine Scripps Institution of Oceanography, University of California, La Jolla, CA, 92093-0204, USA
SOURCE: Angewandte Chemie, International Edition (2003), 42(3), 355-357
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
A member of the "Salinospora" group was examined and was found that strain CNB-392 produces the chemical unique and highly bioactive metabolite salinosporamide A. Salinosporamide A exhibits potent cancer cell cytotoxicity and appears to exert its cytotoxic effects through inhibition of the 20S proteasome. "Salinospora" strain CNB-392 was isolated from a heat-treated marine sediment sample that was plated on sea-water-based agar nutrient medium. Salinosporamide A appears to be a direct product of the fermentation rather than a subsequent transformation product of a precursor similar in structure to that of lactacystin. Salinosporamide A displayed potent in vitro cytotoxicity against HCT-116 human colon carcinoma with an IC50 value of 11 ng/mL. This compound also displayed potent and highly selective activity in the NCI's 60-cell-line panel with a mean GI50 value (the concentration required to achieve 50% growth inhibition) of less than 10 nM and a greater than 4 log LC50 differential between resistant and susceptible cell lines. The unique functionalization of the core bicyclic ring structure of salinosporamide A appears to have resulted in a mol. that is a significantly more potent proteasome inhibitor than omuralide.

IT **437742-34-2**, Salinosporamide A
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(salinosporamide A: highly cytotoxic proteasome inhibitor from novel microbial source, marine bacterium of new genus Salinospora)
RN 437742-34-2 CAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-[(1S)-2-cyclohexen-1-yl]hydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:465746 CAPLUS
DOCUMENT NUMBER: 137:43910
TITLE: Marine actinomycete taxon for drug and fermentation product discovery
INVENTOR(S): Fenical, William; Jenson, Paul R.; Mincer, Tracy J.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

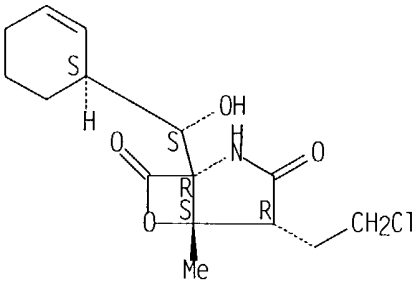
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002047610	A2	20020620	WO 2001-US43758	20011116
WO 2002047610	A3	20021010		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2429163	AA	20020620	CA 2001-2429163	20011116
AU 2002043228	A5	20020624	AU 2002-43228	20011116
US 2003157695	A1	20030821	US 2001-991518	20011116
EP 1341414	A2	20030910	EP 2001-989109	20011116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004535766	T2	20041202	JP 2002-549186	20011116

PRIORITY APPLN. INFO.:
US 2000-249356P P 20001116
WO 2001-US43758 W 20011116

ABSTRACT:
The invention concerns the discovery of an actinomycete genus, given the name Salinospora gen. number, that displays an obligate requirement of the seawater (NA) for growth and unique 16S rRNA signature nucleotides. The invention is also the use of the genus for the production and discovery of active biomols. such as pharmaceutical agents, agrichems., immunomodifiers, enzymes and enzyme inhibitors.

IT **437742-34-2**, Salinosporamide A
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(marine actinomycete taxon for drug and fermentation product discovery)
RN 437742-34-2 CAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 4-(2-chloroethyl)-1-[(S)-[(1S)-2-cyclohexen-1-yl]hydroxymethyl]-5-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

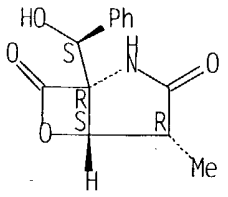
Absolute stereochemistry.



L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:178063 CAPLUS
DOCUMENT NUMBER: 130:296964
TITLE: The structural requirements for inhibition of proteasome function by the lactacystin-derived β-lactone and synthetic analogs
AUTHOR(S): Corey, E. J.; Li, Wei-Dong Z.; Nagamitsu, Tohru; Fenteany, Gabriel
CORPORATE SOURCE: Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA, 02138, USA
SOURCE: Tetrahedron (1999), 55(11), 3305-3316
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The synthesis of analogs of clasto-lactacystin β-lactone in which the substituents at C(5), C(7) and C(9) were systematically varied has led to a well defined structure-activity correlation for the highly selective inhibition of the mammalian 20 S proteasome.

IT **223246-07-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(structural requirements for inhibition of proteasome function by lactacystin-derived β-lactone and synthetic analogs)
RN 223246-07-9 CAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-[(S)-hydroxyphenylmethyl]-4-methyl-, (1R,4R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:12301 CAPLUS
DOCUMENT NUMBER: 126:50959
TITLE: Lactacystin analogs for inhibition of proteasomes and treatment of proteasome-mediated diseases
INVENTOR(S): Schreiber, Stuart L.; Standaert, Robert F.; Fenteany, Gabriel; Jamison, Timothy F.
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 165 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9632105	A1	19961017	WO 1996-US5072	19960412
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RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
US 6335358	B1	20020101	US 1995-421583	19950412
US 5756764	A	19980526	US 1995-466468	19950606
US 6147223	A	20001114	US 1995-468408	19950606
CA 2217817	AA	19961017	CA 1996-2217817	19960412
AU 9655423	A1	19961030	AU 1996-55423	19960412
AU 705791	B2	19990603		
ZA 9602933	A	19970203	ZA 1996-2933	19960412
EP 820283	A1	19980128	EP 1996-912710	19960412
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1187769	A	19980715	CN 1996-194727	19960412
JP 11503732	T2	19990330	JP 1996-531215	19960412
US 6645999	B1	20031111	US 1997-945092	19970126
US 6214862	B1	20010410	US 1997-937228	19970911
US 6458825	B1	20021001	US 2000-639242	20000815
US 2003119887	A1	20030626	US 2001-924993	20010808

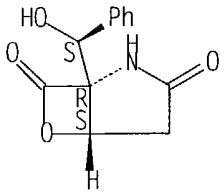
PRIORITY APPLN. INFO.:		
US 1995-421583	A1	19950412
WO 1996-US5072	W	19960412
US 1998-945092	A1	19980126

OTHER SOURCE(S): MARPAT 126:50959
ABSTRACT:
Compds. related to lactacystin and lactacystin β-lactone pharmaceutical compns. containing the compds., and methods of their preparation and use in treatment of proteasome-mediated diseases are claimed.

IT **183873-83-8P**
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of lactacystin analogs for inhibition of proteasomes and

treatment of proteasome-mediated diseases)
RN 183873-83-8 CAPLUS
CN 6-Oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, 1-(hydroxyphenylmethyl)-, [1R-[1α(S*),5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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=> => d his

     (FILE 'HOME' ENTERED AT 11:30:18 ON 21 DEC 2004)

     FILE 'REGISTRY' ENTERED AT 11:30:23 ON 21 DEC 2004
L1             STRUCTURE UPLOADED
L2           0 S L1
L3           7 S L1 FULL

     FILE 'CAPLUS' ENTERED AT 11:30:52 ON 21 DEC 2004
L4           7 S L3
               E FENICAL WILLIAM/AU
L5         303 S E3-E4
               E JENSEN PAUL/AU
L6          95 S E3
               E MINCER TRACY/AU
L7           9 S E3-E4
               E FELING ROBERT/AU
L8           3 S E3-E5
L9         400 S L5 OR L6 OR L7 OR L8
L10          3 S L9 AND SALINO?

=> d que l10 stat
L5         303 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("FENICAL WILLIAM"/AU OR
               "FENICAL WILLIAM H"/AU)
L6          95 SEA FILE=CAPLUS ABB=ON  PLU=ON  "JENSEN PAUL"/AU
L7           9 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("MINCER TRACY"/AU OR "MINCER
               TRACY J"/AU)
L8           3 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("FELING ROBERT"/AU OR "FELING
               ROBERT H"/AU OR "FELING ROBERT H R"/AU)
L9         400 SEA FILE=CAPLUS ABB=ON  PLU=ON  L5 OR L6 OR L7 OR L8
L10          3 SEA FILE=CAPLUS ABB=ON  PLU=ON  L9 AND SALINO?


=> d 1-3 ibib iabs
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L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:570502 CAPLUS
DOCUMENT NUMBER: 141:105361
TITLE: **Salinosporamides** and methods for use thereof
INVENTOR(S): **Fenical, William**; **Jensen, Paul**; **Mincer, Tracy**; **Feling, Robert H. R.**
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 26 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004138196	A1	20040715	US 2003-600854		20030620
PRIORITY APPLN. INFO.:			US 2002-391314P	P	20020624

OTHER SOURCE(S): MARPAT 141:105361
ABSTRACT:
The present invention is based on the discovery that certain fermentation products of the marine actinomycete strains CNB392 and CNB476 are effective inhibitors of hyperproliferative mammalian cells. The CNB392 and CNB476 strains lie within the family Micromonosporaceae, and the generic epithet **Salinospora** has been proposed for this obligate marine group. The reaction products produced by this strain are classified as **salinosporamides**, and are particularly advantageous in treating neoplastic disorders due to their low mol. weight, low IC 50 values, high pharmaceutical potency, and selectivity for cancer cells over fungi.

L10 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:101938 CAPLUS
DOCUMENT NUMBER: 139:81745
TITLE: **Salinosporamide** A: a highly cytotoxic proteasome inhibitor from a novel microbial source, a marine bacterium of the new genus **Salinospora**
AUTHOR(S): **Feling, Robert H.**; Buchanan, Greg O.; **Mincer, Tracy J.**; Kauffman, Christopher A.; Jensen, Paul R.; **Fenical, William**
CORPORATE SOURCE: Center for Marine Biotechnology and Biomedicine Scripps Institution of Oceanography, University of California, La Jolla, CA, 92093-0204, USA
SOURCE: Angewandte Chemie, International Edition (2003), 42(3), 355-357
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
A member of the "**Salinospora**" group was examined and was found that strain CNB-392 produces the chemical unique and highly bioactive metabolite ***salinosporamide*** A. **Salinosporamide** A exhibits potent cancer cell cytotoxicity and appears to exert its cytotoxic effects through inhibition of the 20S proteasome. "**Salinospora**" strain CNB-392 was isolated from a heat-treated marine sediment sample that was plated on sea-water-based agar nutrient medium. **Salinosporamide** A appears to be a direct product of the fermentation rather than a subsequent transformation product of a precursor similar in structure to that of lactacystin. **Salinosporamide** A displayed potent in vitro cytotoxicity against HCT-116 human colon carcinoma with an IC50 value of 11 ng/mL. This compound also displayed potent and highly selective activity in the NCI's 60-cell-line panel with a mean GI50 value (the concentration required to achieve 50% growth inhibition) of less than 10 nM and a greater than 4 log LC50 differential between resistant and susceptible cell lines. The unique functionalization of the core bicyclic ring structure of ***salinosporamide*** A appears to have resulted in a mol. that is a significantly more potent proteasome inhibitor than omuralide.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:465746 CAPLUS
DOCUMENT NUMBER: 137:43910
TITLE: Marine actinomycete taxon for drug and fermentation product discovery
INVENTOR(S): **Fenical, William**; Jenson, Paul R.; **Mincer, Tracy J.**
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002047610	A2	20020620	WO 2001-US43758	20011116
WO 2002047610	A3	20021010		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2429163	AA	20020620	CA 2001-2429163	20011116
AU 2002043228	A5	20020624	AU 2002-43228	20011116
US 2003157695	A1	20030821	US 2001-991518	20011116
EP 1341414	A2	20030910	EP 2001-989109	20011116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004535766	T2	20041202	JP 2002-549186	20011116
PRIORITY APPLN. INFO.:			US 2000-249356P P	20001116
			WO 2001-US43758 W	20011116

ABSTRACT:
The invention concerns the discovery of an actinomycete genus, given the name ***Salinospora*** gen. number, that displays an obligate requirement of the seawater (NA) for growth and unique 16S rRNA signature nucleotides. The invention is also the use of the genus for the production and discovery of active biomols. such as pharmaceutical agents, agrichems., immunomodifiers, enzymes and enzyme inhibitors.